

CLAIMS

- 5 1. Apparatus for obtaining an image of a specimen by optical projection tomography, the apparatus comprising light scanning means and a rotary stage for rotating the specimen to indexed positions in each of which the specimen is in use subjected to a scanning movement of incident light by the scanning means.
- 10 2. Apparatus according to claim 1, wherein the incident light is scanned in a direction perpendicular to an optical axis followed by the light passing through the apparatus.
3. Apparatus according to claim 1 or 2, wherein the incident light is scanned in a raster pattern, one complete scan being undertaken at each indexed position of the specimen.
- 15 4. Apparatus according to any of the preceding claims, wherein the light scanning means form part of a confocal scanning microscope.
5. A method of obtaining an image of a specimen by optical projection tomography, comprising scanning the specimen with a light beam and detecting light emanating from the specimen to derive the image.
- 20 6. A method according to claim 5, wherein the light passes through the specimen prior to being detected.
- 25 7. A method according to claim 5, wherein the light enters from one side of the specimen and leaves the specimen from the same side thereof.
8. A method according to any of claims 5 to 7, wherein the specimen is rotated to indexed positions and one complete scan is undertaken at each indexed position of the specimen.
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9. A method according to any of claims 5 to 7, wherein the detector detects light which exits or by-passes the specimen parallel to the beam incident on the specimen.

5 10. A method according to any of claims 5 to 9, wherein the light is laser light.

11. A method of performing any one or more of the analyses or procedures listed hereunder comprising use of a method or apparatus according to any of claims 1 to 10:

10 Analysis of the structure of biological tissues.

Analysis of the function of biological tissues.

Analysis of the shapes of biological tissues.

Analysis of the distribution of cell types within biological tissues.

Analysis of the distribution of gene activity within biological tissues,

15 including the distribution of:

- RNA transcripts

- proteins

Analysis of the distribution of transgenic gene activity within biological tissues,

Analysis of the distribution of cell activities within biological tissues,

20 including:

- Cell cycle status including arrest

- Cell death

- Cell proliferation

- Cell migration

25 Analysis of the distribution of physiological states within biological tissues.

Analysis of the results of immunohistochemistry staining techniques.

Analysis of the results of in-situ hybridisation staining techniques.

Analysis of the distribution of molecular markers within biological tissues,

including any coloured or light-absorbing substances, such as:

30 5,5'-dibromo-4,4'-dichloro-indigo (or other halogenated indigo compounds)
formazan

or other coloured precipitates generated through the catalytic activity of enzymes including: b-galactosidase, alkaline phosphatase or other coloured precipitates formed upon catalytic conversion of staining substrates,

including: Fast Red, Vector Red

5 And including any light-emitting substances,

Therefore including any fluorescent substances,

such as: Alexa dyes, FITC, rhodamine,

And including any luminescent substances,

such as green fluorescent protein (GFP) or similar proteins,

10 And including any phosphorescent substances.

Analysis of tissues from all plant species.

Analysis of any tissue for agricultural research,

including:

15 basic research into all aspects of plant biology (genetics, development, physiology, pathology etc.)

analysis of tissues which have been genetically altered.

Analysis of tissues from all animal species.

20 including:

invertebrates

nematode worms

vertebrates

25 all types of fish (including teleosts, such as zebrafish, and chondrycthes including sharks)

amphibians (including the genus *Xenopus* and axolotls)

reptiles

birds (including chickens and quails)

30 all mammals (including all rodents, dogs, cats and all primates, including human)

Analysis of embryonic tissues for any purpose,

including:

research into any stem cell population

research into developmental biology

research into the causes of abnormal embryo development, including human
syndromes

autopsies of human terminated pregnancies (both spontaneous and induced
terminations)

Analysis of any tissues for the purpose of genomics research,

including:

the analysis of any tissues for the purpose of genomics research,

including:

the analysis of transgenic, knock-in, knock-down or knock-out organisms

the analysis or discovery of the expression (or activity) of genes including
their spatial distribution, and their levels of expression

the analysis of discovery of abnormalities in the structure or morphology of
tissues, as a result of interference due to wilful experimentation (such as
genetic or physical modifications including a chemical or biochemical
genomics approach), and/or spontaneous abnormalities (such as naturally-
occurring mutations)

Analysis of any tissue for the purpose of neurobiology research,

including:

the analysis of the morphology of nerves

the analysis of the pathways and connectivity of nerves

the analysis of parts of, or whole, animal brains

Analysis of any tissue for pharmaceutical research,

including:

the analysis of pharmaceutical substances (such as drugs, molecules, proteins,
antibodies),

including their spatial distribution within the tissue, and their concentrations
the analysis or discovery of abnormalities in the structure or morphology of tissues.

Analysis of tissues for medical research,

5 including:

research into the genetics, development, physiology, structure and function of
animal tissues

analysis of diseased tissue to further our understanding of all types of diseases

including:

10 congenital diseases

acquired diseases

including:

infectious

neoplastic

15 vascular

inflammatory

traumatic

metabolic

endocrine

20 degenerative

drug-related

iatrogenic or

idiopathic diseases

25 Analysis of tissues for medical diagnosis, treatment or monitoring,
including:

the diagnosis of cancer patients

including:

searching for cancerous cells and tissues within biopsies

30 searching for abnormal structure or morphology of tissues within biopsies

the analysis of all biopsies

including the analysis of:

lymph nodes

polyps

liver biopsies

5 kidney biopsies

prostate biopsies

muscle biopsies

brain tissue

the analysis of tissue removed in the process of extracting a tumour from a patient

10 including:

determining whether all the tumour has been removed

determining the type of tumour, and the type of cancer.

12. Use of a method or apparatus as described in any of claims 1 to 10 in any one or
15 more of the analyses or procedures listed hereunder:

Analysis of the structure of biological tissues.

Analysis of the function of biological tissues.

Analysis of the shapes of biological tissues.

20 Analysis of the distribution of cell types within biological tissues.

Analysis of the distribution of gene activity within biological tissues,

including the distribution of:

- RNA transcripts

- proteins

25 Analysis of the distribution of transgenic gene activity within biological tissues,

Analysis of the distribution of cell activities within biological tissues,

including:

- Cell cycle status including arrest

- Cell death

30 - Cell proliferation

- Cell migration

Analysis of the distribution of physiological states within biological tissues.

Analysis of the results of immunohistochemistry staining techniques.

Analysis of the results of in-situ hybridisation staining techniques.

Analysis of the distribution of molecular markers within biological tissues,

5 including any coloured or light-absorbing substances, such as:

5,5'-dibromo-4,4'-dichloro-indigo (or other halogenated indigo compounds)
formazan

or other coloured precipitates generated through the catalytic activity of enzymes

including: b-galactosidase, alkaline phosphatase or other coloured precipitates formed upon

10 catalytic conversion of staining substrates,

including: Fast Red, Vector Red

And including any light-emitting substances,

Therefore including any fluorescent substances,

such as: Alexa dyes, FITC, rhodamine,

15 And including any luminescent substances,

such as green fluorescent protein (GFP) or similar proteins,

And including any phosphorescent substances.

Analysis of tissues from all plant species.

20 Analysis of any tissue for agricultural research,

including:

basic research into all aspects of plant biology (genetics, development, physiology,
pathology etc.)

analysis of tissues which have been genetically altered.

25

Analysis of tissues from all animal species.

including:

invertebrates

nematode worms

30

vertebrates

all types of fish (including teleosts, such as zebrafish, and chondrycthes including sharks)

amphibians (including the genus *Xenopus* and axolotls)

reptiles

5 birds (including chickens and quails)

all mammals (including all rodents, dogs, cats and all primates, including human)

Analysis of embryonic tissues for any purpose,
including:

10 research into any stem cell population

research into developmental biology

research into the causes of abnormal embryo development, including human syndromes

15 autopsies of human terminated pregnancies (both spontaneous and induced terminations)

Analysis of any tissues for the purpose of genomics research,
including:

the analysis of any tissues for the purpose of genomics research,

20 including:

the analysis of transgenic, knock-in, knock-down or knock-out organisms

the analysis or discovery of the expression (or activity) of genes including their spatial distribution, and their levels of expression

25 the analysis of discovery of abnormalities in the structure or morphology of tissues, as a result of interference due to wilful experimentation (such as genetic or physical modifications including a chemical or biochemical genomics approach), and/or spontaneous abnormalities (such as naturally-occurring mutations)

30 Analysis of any tissue for the purpose of neurobiology research,
including:

the analysis of the morphology of nerves

the analysis of the pathways and connectivity of nerves

the analysis of parts of, or whole, animal brains

5 Analysis of any tissue for pharmaceutical research,

including:

the analysis of pharmaceutical substances (such as drugs, molecules, proteins, antibodies),

including their spatial distribution within the tissue, and their concentrations

10 the analysis or discovery of abnormalities in the structure or morphology of tissues.

Analysis of tissues for medical research,

including:

15 research into the genetics, development, physiology, structure and function of animal tissues

analysis of diseased tissue to further our understanding of all types of diseases

including:

congenital diseases

acquired diseases

20 including:

infectious

neoplastic

vascular

inflammatory

25 traumatic

metabolic

endocrine

degenerative

drug-related

30 iatrogenic or

idiopathic diseases

Analysis of tissues for medical diagnosis, treatment or monitoring,
including:

the diagnosis of cancer patients

5 including:

searching for cancerous cells and tissues within biopsies

searching for abnormal structure or morphology of tissues within biopsies

the analysis of all biopsies

including the analysis of:

10 lymph nodes

polyps

liver biopsies

kidney biopsies

prostate biopsies

15 muscle biopsies

brain tissue

the analysis of tissue removed in the process of extracting a tumour from a patient

including:

determining whether all the tumour has been removed

20 determining the type of tumour, and the type of cancer.